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## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:  
M. Seul et al.

Serial No. 09/448,420

Filed: 11/22/1999

For: Color-Encoding and *in-situ*  
Interrogation of Matrix-Coupled  
Chemical Compounds

Group Art Unit: 1639

Examiner: P. Ponnaluri

I hereby certify that, on the date indicated below, this  
correspondence was sent by fax to the Commissioner  
for Patents, at (703) 872-9306.By: 

Date: 4/3/04

Commissioner for Patents  
PO Box 1450  
Alexandria VA 22313-1450

## Reply Brief to Examiner's Answer

Dear Sir:

Applicants hereby request an oral hearing in this matter. Please charge the \$140.00 fee associated with this request to Deposit Account No. 502088.

## Background and Introduction

Applicants repeatedly emphasized in their Brief that step (g) of claim 129, which recites, "decoding the code composed of one or more tag(s) to identify the compound ... wherein said decoding step comprises *in-situ* optical interrogation of the tag(s)," does *not* mean identify "*the bead*" associated with the compound (as the Examiner implies), nor does it mean identify compounds having "a property of interest" (as the Examiner also

implies), as compounds having “a property of interest” are *indicated* in step (f), and the *decoding* of the identity of such compounds is described in step (g). Applicants emphasized that the term “the code” in step (g) (*i.e.*, “decoding *the code* composed of one or more tag(s) ...”) only appears in step (g) and in step (c), and not in step (f).<sup>1</sup> In addition, the term “optical interrogation” appears only in steps (g) and (c) and not in step (f). Accordingly, the meaning of “the code” and “optical interrogation” must be construed with reference to step (c) and (g), and step (f) is not relevant to their construction and is not in any way referred to by use of these terms. The Examiner (now joined by the SPE and the Biotech Practice Specialist) refuses to acknowledge that different words in different parts of the claim have different meanings.

Step (c) reads as follows:

(c) adding to one or more batches, prior to (b), concurrently with (b), or subsequently to (b), one or more tag(s), each tag able to be attached to the solid support and able to be identified by optical interrogation, wherein said one or more tag(s) constitutes a code, ***which code is uniquely associated with a compound and a corresponding reaction sequence and is determined by optical interrogation*** [emphasis added]

Notwithstanding the terms in the steps described in steps (c) and (g), and “performing an assay” described in wholly different terms in step (f), the Examiner continues to insist that “decoding the code composed of one or more tag(s) to identify the compound associated with the code ...” in step (g) means determining the results of the assay performed in step (f) (*i.e.*, identifying “the bead,” according to the Examiner, and/or finding compounds having “a property of interest”). The Examiner also continues to insist that when, in the references, an assay is performed which *indicates* a property of

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<sup>1</sup> Step (f) recites: “performing an assay capable of indicating that any compound in the library has a property of interest ...”

interest by an optically detectable change (in a manner analogous to the assay procedure described in step (f) which can indicate that a “compound in the library has a property of interest ...”), this is the “optical interrogation” which is referred to in steps (g) and (c), notwithstanding the clear language in step (c) that optical interrogation is used to determine *the code* “*uniquely associated with a compound* and a corresponding reaction sequence...” and notwithstanding the language in step (g): “decoding *the code* composed of one or more tag(s) *to identify the compound* associated with *the code* ... wherein said decoding step comprises *in-situ optical interrogation* of the tag(s).” In view of the record in this matter, and the Examiner’s statements in the Answer, it is clear that the Examiner is deliberately misquoting the pertinent claim language in an attempt to mislead the Board. Several examples of such deliberate misquotes are set forth in Section A. below.

#### **A. The Examiner Misquotes the Claim Language In Attempting to Mislead**

##### **Examiner’s Answer, p. 13, 2d paragraph:**

Dower et al. teach “after the receptor assay (the receptor assay refers to the instant claim step (f)) the positive beads (identify the compound of interest) are identified and isolated using fluorescent activated solid support sorting (which refers to the instant claim *decoding the tag to identify the compound*, wherein decoding comprises *optical interrogation*.)

Step (g) actually recites: “decoding *the code* composed of one or more tag(s) to identify the compound associated with the code ...” and the term “the code” does not refer to or appear in claim step (f). But by misquoting step (g) as “decoding the tag to identify the compound” the Examiner is attempting to make it appear that decoding using optical interrogation in step (g), does, or could, refer to indicating the “positive beads” resulting

from the assay in step (f). The “code” appears only in steps (c) and (g) and not in step (f), and the use of “tag” in the context of the argument by the Examiner above is an attempt to mislead. Also, in step (g), “decoding” using “in-situ optical interrogation” is used to “identify the compound associated with the code” – not the positive beads associated with “compounds of interest” as the Examiner implies.

**Examiner’s Answer, p. 14, 2d paragraph:**

However, the instant claims only recite “in situ optical interrogation to identify the compound” and the limitation “to identify the sequence or structure of the compound attached to the bead” is not part of the claim.

Step (g) actually recites: “wherein said *decoding step* comprises in-situ optical interrogation of the tag(s),” and, in step (g), the “decoding step” refers to the first phrase in step (g) “decoding the code ...”, and step (c) states that the “code is uniquely associated with a compound and a corresponding reaction sequence and is determined by optical interrogation ...” By deleting the term “decoding” from the quoted passage, the Examiner is clearly attempting to mislead the Board into believing that the code is somehow *not* “uniquely associated with a compound and a corresponding reaction sequence...” as is set forth in step (c), and that an additional limitation (“to identify the sequence or structure of the compound attached to the bead”) must be added to the claim to distinguish steps (g) and (f).

**Examiner’s Answer, p. 14, last sentence, to p.15:**

Applicants assertions ... are not persuasive because, the instant claim step (g) recites “decoding to identify the compound associated with the code” which refers to identification of positive bead with the compound attached to the bead.

Step (g) actually recites: “decoding *the code* composed of one or more tag(s) to identify the compound associated with the code ...” Step (c) recites that the “*code* is uniquely

associated with a compound and a corresponding reaction sequence and is determined by optical interrogation ...” and thus, step (g) clearly does not refer to “identification of positive bead,” as this is performed in assay step (f). The Examiner’s omission of “the code” from the quoted passage of step (g) is another example of an attempt to mislead the Board into believing that “decoding” can refer to “identification of positive beads.”

**Examiner’s Answer, p. 15, first paragraph:**

In the instant claim step (c) recites the property of the code (i.e., capable of determining reaction sequence by optical interrogation) used in the claimed method, however the method steps, especially step g, does not recite the reaction sequence or the structure or sequence of the compound attached to the bead is identified by in-situ optical interrogation.

Step (c) actually recites: “wherein said one or more tag(s) constitutes a code, which code *is uniquely associated with a compound and a corresponding reaction sequence* and is determined by optical interrogation ...” The Examiner failed to note (apparently deliberately) that step (c) states that the code is uniquely associated with *both* a reaction sequence *and* a compound. Accordingly, when you “decode the code” in step (g), you determine the reaction sequence and you *uniquely identify* the compound.

**Examiner’s Answer, p. 16, first full paragraph:**

And the reference teaches after synthesis is completed, the reaction products are screened for desired property by incubating the beads with fluorescently labeled antibody ... which refers to the in-situ optical interrogation of the beads to identify the compound with desired biological property of the instant claims.

Step (g) of the “instant claims” actually states: “wherein *said decoding step* comprises *in-situ optical interrogation* of the tag(s),” and, in step (g), the “decoding step” refers to the first phrase in step (g) “decoding the code ...”, and step (c) states that the “code is uniquely associated with a compound and a corresponding reaction sequence and is

determined by optical interrogation ...” By making it appear that the terms “decoding,” “the code,” “tags,” are not present in step (g), and that step (g) states something about “in-situ optical interrogation of the beads” to determine a “biological property,” the Examiner is attempting to mislead the Board into believing that step (g) “optical interrogation” refers to assay step (f).

**Examiner’s Answer, p. 16, first full paragraph, last sentence:**

This is not persuasive, since the teachings of Still et al. identification of positive beads with fluorescent tag (refers to the instant tag) from among other beads, refers to decoding to identify the compound, ... wherein said decoding step comprises in-situ optical interrogation of the tag, of the instant claims.

Again, by using the term “decoding to identify the compound” instead of “*decoding the code*” composed of one or more tag(s) to identify the compound associated with the code ... “ as in step (g), the Examiner is attempting to mislead the Board into believing that the term “the code” (clearly defined in step (c) as uniquely identifying a compound and its reaction sequence), is not present in step (g), and that “decoding” using “in-situ optical interrogation” could refer to “identification of positive beads” (in the words of the Examiner), which is another way of saying: indicating a compound having a property of interest, as in assay step (f).

**Examiner’s Answer, p. 16, last line, to page 17:**

Applicants’ assertions ... are not persuasive because, the instant claim step (g) recites “decoding to identify the compound associated with the code” refers to identification of positive bead with the compound attached to the bead.

Again, by using the term “decoding to identify the compound” instead of “*decoding the code*” composed of one or more tag(s) to identify the compound associated with the code ... “ as in step (g), the Examiner is attempting to mislead the Board into believing that the term “decoding” could refer to “identification of positive beads,” (in the words of the

Examiner), which is another way of saying: indicating a compound having a property of interest, as in assay step (f).

**Examiner's Answer, p. 20, last paragraph:**

Dower et al. clearly teach 'after the receptor assay (the receptor assay refers to the instant claim step (f)), the positive beads (identify the compound of interest) are identified and isolated using fluorescent activated cell sorting, which refers to the instant claim decoding the tag to identify the compound, wherein the decoding comprises optical interrogation.

By making it appear as if step (g) recites: "decoding *the tag* [it really states: "*the code*"] to identify the compound, wherein the decoding comprises optical interrogation..." the Examiner is attempting to mislead the Board into thinking that the term "code" is not present in step (g), and "decoding" using "optical interrogation" in step (g) could refer to "identification of positive beads" (in the words of the Examiner), which is another way of saying: indicating a compound having a property of interest, as in assay step (f).

**B. Realizing that a Number of Claim Elements Are Not Present in the References, the Examiner Elected not to Comply with the Rules in Drafting the Examiner's Answer**

MPEP Section 1208(A)(10), subparts (c)&(e), respectively require:

(c) For each rejection under 35 U.S.C. 102, the examiner's answer, or single prior action, shall explain why the rejected claims are anticipated or not patentable under 35 U.S.C. 102, pointing out where *all of the specific limitations recited in the rejected claims are found in the prior art relied upon in the rejection.* [emphasis added]

(e) For each rejection under 35 U.S.C. 102 or 103 where there are questions as to how limitations in the claims correspond to features in the prior art even after the examiner complies with the requirements of paragraphs (c) and (d) of this section, *the examiner shall compare at least one of the rejected claims feature by feature with the prior art relied on in the rejection. The comparison shall align the language of the claim side-by-side with a reference to the specific page, line*

*number, drawing reference number, and quotation from the prior art, as appropriate.* [emphasis added]

The Examiner has failed to make any such required comparison in the Answer, because the Examiner is fully aware that such comparison renders the rejections unsupportable.

Claim 129, from the beginning through step (f), reads as follows:

129. A method of identifying a compound of interest in a library of compounds, each of said compounds being bound to a solid support and being produced by a unique reaction series composed of N reaction steps, wherein N is an integer of at least 2, and wherein each compound is produced from components which are independently the same or different, the method comprising:

- (a) dividing a population of solid support into M batches, wherein M is an integer greater than 1;
- (b) reacting each of the M batches of solid support with a component, so that the component forms a bond with the solid support;
- (c) adding to one or more batches, prior to (b), concurrently with (b), or subsequently to (b), one or more tag(s), each tag able to be attached to the solid support and able to be identified by optical interrogation, wherein said one or more tag(s) constitutes a code, which code is uniquely associated with a compound and a corresponding reaction sequence and is determined by optical interrogation;
- (d) recombining all of said M batches after (b) and (c);
- (e) repeating (a) to (d) for N-1 times, or repeating (a) to (d) for N-2 times followed by repeating (a) to (c) once, to produce a library of compounds;
- (f) performing an assay capable of indicating that any compound in the library has a property of interest...

If the Examiner is correct in the assertion that "decoding the code" in step (g) can properly refer to a "code" which is used to indicate compounds with "a property of interest" in the assay of step (f), and that "optical interrogation" in step (g) is used to "decode and identify" such compounds with "a property of interest," then, at least one of the Section 102 references must disclose that: following encoding of compounds with such "code" (pursuant to step (c)), the steps required in claim 129 (d) and (e) are



performed on such encoded compounds. But none of the Section 102 references (Boyce et al., Dower et al. and Still et al.) disclose that *following establishing a code for compounds with "a property of interest,"* the batches of encoded compounds are recombined (as required in step (d)), and then, that the "divide" "react" "encode" and "recombine" steps required in step (e) are performed.<sup>2</sup> This is because in these references, as in step (f), an assay is performed to determine compounds with "a property of interest," and encoding (and "decoding") is performed separately to permit identification of individual members of a library of synthesized compounds and their reaction sequences. Upon realizing that these required elements were missing from the references, the Examiner chose not to match up the claim elements against the applicable portions of the prior art references, as required in the applicable rules. But because these claim elements are missing in the prior art, and because the Examiner has never even alleged that they are present in the prior art, it is clear that, for this reason alone, all the Section 102 rejections are unsupported and must be reversed.

### C. The Section 103(a) Rejection Is Baseless

The Examiner has maintained the Section 103(a) rejection, although it is noted that the rejection stands or falls based on whether Dower et al. is interpreted as advocated by the Examiner, *i.e.*:

Dower et al. clearly teach "after the receptor assay (the receptor assay refers to the instant claim step (f)), the positive beads (identify the compound of interest) are identified and isolated using fluorescent activated solid support sorting, which

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<sup>2</sup> Of course, it would make no sense to first encode the compounds with "a property of interest," and then recombine separate batches, and then "divide" "react" "encode" and "recombine" again, because the encoded compounds would be altered by the next reaction round, and those encoded as "of interest" might no longer be "of interest," thereby rendering the code useless.

refers to the instant claim decoding the tag to identify the compound, wherein the decoding comprises optical interrogation. [Answer, page 20, last sentence]

As noted above, step (g) does not state "decoding the tag to identify the compound..." but rather "decoding the code composed of one or more tag(s) to identify the compound associated with the code..." and "code" is clearly defined as uniquely associated with a compound and a reaction sequence in step (c), and is not mentioned in the "performing an assay" step (f). Accordingly, because the Examiner's interpretation of Dower et al. is wholly inconsistent with the claim language, in addition to all the other reasons listed in the Brief, the rejection should be reversed.

Also, for the same reasons noted above in part B that the Section 102 rejections are not supported (*i.e.*, claim steps (d) and (e) are not alleged as being in any reference), the Section 103 rejection is unsupported. The primary reference supporting the Section 103 rejection is Dower et al., which does not disclose that following establishing a code for compounds with "a property of interest," the batches of encoded compounds are recombined (as required in step (d)), and then, that the "divide" "react" "encode" and "recombine" steps required in step (e) are performed. Combining Dower et al. with Metzker et al. does not, therefore, yield the claimed invention. Again, it is noted that the MPEP rule 1208 requires that, for a Section 103 rejection where the correspondence between claim and prior art is questioned, the claim be specifically aligned with the prior art, and that was not done in the Answer.

The Examiner also states that: "one cannot show nonobviousness by attacking references individually where the rejections are based on a combination of references. See *In re Keller*... *In re Merck & Co.*..." Of course, this statement is completely

incorrect, and does not reflect the holdings of these decisions; otherwise one would never be able to overcome a rejection under Section 103(a). A better summary of the holding is: "One cannot show nonobviousness by selecting the portions of certain references that support such position and ignoring others that undercut such position." This was clearly not done (and the Examiner has never alleged it was done) by Applicants, who have considered and discussed the cited references extensively in their Brief.

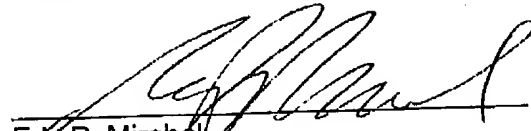
In view of the Examiner's actions in this matter, including misquoting the claims to attempt to mislead the Board, and not complying with the rules requiring a comparison of the claim language to the references because such comparison would expose the error of her position, Applicants request that the Board not penalize Applicants further in this matter, and reverse these wholly improper and unsupported rejections, or render a remand which is a "final decision" so that Applicants would not, in addition to the delays already suffered, end up unable to receive an extension of patent term to compensate for the time lost pursuing this appeal. Finally, Applicants wish to apologize to the Board for having to spend its time on this matter, which clearly should have been resolved by allowance and without an appeal.

Respectfully

Submitted,

Dated: 4/26/2004

By:

  
Eric P. Mirabel  
Registration No. 31,211

Correspondence Address::  
Bioarray Solutions  
35 Technology Drive  
Warren New Jersey 07059  
Telephone 908 226 8200 Ext 203  
Facsimile: 908 226 0800